Health Effects in Army Gulf War Veterans Possibly Exposed to Chemical Munitions Destruction at Khamisiyah, Iraq: Part I. Morbidity Associated with Potential Exposure

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In March 1991, U.S. troops detonated the Khamisiyah, Iraq, ammunition depot, possibly releasing two chemical warfare agents, sarin and cyclosarin. The long-term health effects associated with possible exposure to these chemical warfare agents are unknown. This study was undertaken to investigate whether possible exposure was associated with morbidity among Army Gulf War veterans using morbidity data for 5,555 Army veterans who were deployed to the Gulf region. Responses to 86 self-assessed health measures, as reported in the 1995 Department of Veterans Affairs National Health Survey of Gulf War Era Veterans, were evaluated. We found little association between potential exposure and health, after adjustment for demographic variables, and conclude that potential exposure to sarin or cyclosarin at Khamisiyah does not seem to have adversely affected self-perceived health status, as evidenced by a wide range of health measures.

Introduction

Immediately after the Gulf War, demolition was carried out in March 1991 at the Khamisiyah ammunition depot in southeastern Iraq. Troops who were possibly exposed to chemical warfare agents were identified subsequently by environmental and climatological modeling, in conjunction with unit location data for the days of the demolition.[1] In this article, we compare the morbidity outcomes in the group of Army veterans possibly exposed to low levels of chemical warfare agents with those of a similar group of unexposed Army personnel. The morbidity data were collected as part of the Department of Veterans Affairs (VA) National Health Survey of Gulf War Era Veterans (NHS).[2] Two other articles examine deaths associated with possible exposure[3] and morbidity associated with notification of possible exposure.[4]

On March 4 and 10, 1991, combat engineer and explosive ordnance disposal units of the U.S. Army XVIII Corps (Airborne) destroyed two large caches of 122-mm rockets, one in a bunker and the other in a nearby pit, at the Khamisiyah ammunition supply point, ~350 km southeast of Baghdad, Iraq. In October 1991, March 1992, May 1992, and May 1998, representatives from the United Nations Special Commission inspected Khamisiyah and detected the existence of sarin and cyclosarin in both intact and damaged rockets in the bunker and pit.[1]

Approximately contemporaneously, concerns increased about postwar morbidity among Gulf War veterans.[5-12] On June 21, 1996, the Department of Defense (DoD) released a statement confirming that U.S. soldiers had destroyed ammunition bunkers at Khamisiyah, Iraq, and that one of these bunkers contained chemical warfare agents.[13] Following this, the DoD made efforts to determine who was possibly exposed to chemical agents (see below) and also made efforts to notify veterans of possible exposure; the effects of these notification letters are the subject of another article.[4]

Toxicology of Nerve Agents Sarin and Cyclosarin

Sarin, an organophosphorus ester, is a highly toxic nerve agent. Exposure to acutely toxic concentrations can produce excessive bronchial, salivary, ocular, and intestinal secretions, as well as sweating, miosis, bronchospasm, bradycardia, muscle fasciculations, paralysis, convulsions, and death.[14] Minimal effects observed at low concentrations include miosis, chest tightness, rhinorrhea, and dyspnea.[14] There is limited evidence associating sarin exposure at a level sufficient to produce acute cholinergic signs with subsequent long-term health effects, such as fatigue, headache, blurred vision, post-traumatic stress disorder (PTSD), and abnormal test results of unknown clinical significance.[15] At doses too low to produce acute cholinergic effects, there is insufficient evidence to determine whether there is an association with subsequent long-term health effects, in part because of a lack of well-controlled studies.[15] Cyclosarin is similar in composition to sarin, although less volatile. Its mechanism of action is similar to that of sarin, although less is known about its toxicity.[15] A recent study of self-reported, long-term (25–45 years), health effects among 1,339 veterans experimentally exposed to anticholinesterase agents (including 287 exposed to sarin) included neurological and psychological outcomes such as peripheral nerve disease, vestibular dysfunction, sleep disorders, anxiety, and depression. There were only two statistically significant differences, i.e., subjects exposed to anticholinesterase agents had fewer attention problems than subjects in one control group and greater sleep disturbance problems than subjects in another control group. In contrast, self-reported exposure to hazardous chemicals outside the experimental testing program was significantly associated with all primary study outcomes.[16]

Methods

Study Population

The cohort for this study was selected in collaboration with the Office of the Special Assistant for Gulf War Illnesses, the

Deployment Environmental Surveillance Program of the U.S. Army Center for Health Promotion and Preventive Medicine, and the VA Environmental Epidemiology Service. Eligibility for entry into the cohort was based on the veteran having served in the Gulf theater of operations. Individuals identified as having been within and outside the modeled potential hazard area were eligible for inclusion. The cohort was further defined by having participated in Phase I of the VA NHS, conducted in 1995–1997.[2]

The NHS was designed as a retrospective cohort study in which health factors of a population-based sample of 15,000 troops deployed into the Gulf area were compared with those of 15,000 troops serving in the military during the period of the Gulf War but not in the Gulf area. Phase I of the survey was performed in 1995–1996, before troop notification of possible chemical agent exposure at Khamisiyah, Iraq, by the DoD. A total of 11,441 military personnel, who represented four branches of service deployed to the Gulf region during the 1990–1991 Gulf War, responded to either Phase I, the postal printed questionnaire survey in 1995–1996, or Phase II, the telephone interview survey in 1996–1997. The subset of veterans who participated in the postal questionnaire survey and who served in the Army numbered 5,555.

Determining Possible Exposure

The risk factors associated with the demolition in the Khamisiyah pit in March 1991 are possible exposures to chemical warfare agents, including sarin and cyclosarin.[1] For completeness, we also examined the data using exposure defined with the "50-km model," an early exposure model that declared Gulf War veterans who were within a circle with a radius of 50 km, centered at Khamisiyah, Iraq, to have been possibly exposed.[1] The history of DoD's exposure determination efforts is given below in brief.

Determining the possible risk of chemical agent exposure to U.S. troops in the vicinity of Khamisiyah began as a joint effort by the Central Intelligence Agency and the DoD in late 1996. It quickly became apparent that the pit demolition posed a number of challenges requiring expertise in modeling the physical characteristics of open-air demolition, as well as environmental and meteorological conditions at the site. The DoD-Central Intelligence Agency team used interviews with troops who had been at the site and test demolitions and other experiments at the Dugway Proving Grounds and Edgewood Laboratories to reduce uncertainties associated with the physical and environmental conditions at the site. Because of relatively scarce meteorological data for Iraq, the team used state-of-the-art mesoscale meteorological models to simulate prevailing weather conditions over the region. Dispersion models were then used to predict the transport and spread of chemical warfare agents, based on these simulated meteorological conditions. To account for uncertainty, a conservative assumption was made to define the potential hazard area as the union of the hazard areas given by each of the various combinations of meteorological and dispersion models. The result was the generation of a potential hazard area that varied in size and shape from March 10 to March 13, 1991. From this, the team was able to determine which units of troops were presumed to have been within the potential hazard area over the course of the 4-day period. The result of this effort is known as the "1997 hazard area" (see Ref. 1 for additional details).

Several factors contributed to the development of a subsequent exposure model, the remodeling effort or the "2000 hazard area." Meteorological modeling methods were further refined. The assumed amount of nerve agent released was reduced, based on more-recent intelligence analyses. The toxicity effects of cyclosarin were added to those of sarin, which was used alone in the 1997 analysis. Atmospheric removal mechanisms, such as dry deposition and degradation, were also considered. Finally, and possibly of most importance, unit location information was significantly improved in the 2000 model. Both models considered a soldier to have been exposed if his or her unit was in the hazard area but in 1997 the unit was generally at the battalion level (~1,000 soldiers), whereas in 2000 the unit was generally at the company level (~200 soldiers). Therefore, on average, an individual's unit was located with greater precision in the 2000 hazard area. In this study, an individual is deemed presumed exposed if, during any of the four 24-hour periods from March 10 to March 13, 1991, his or her unit was at a location that was exposed to a level of chemical warfare agent higher that the general population limit, adjusted for short-term exposure.[1] The general population limit is defined as the limit below which any member of the general population could be exposed daily, for a lifetime, and not experience any related adverse health effects. The modeling process also provided data on the number of days (0 or 1 through 4) of potential exposure. Although this does not constitute a true measure of intensity of exposure, we used number of days of exposure in some of our analyses as a limited proxy for intensity of exposure. We adopt the terms "exposed" to mean possible exposure under the 2000 hazard area, "unexposed" to mean no exposure under the 2000 hazard area, and "missing exposure" to mean that there was no 2000 hazard area exposure status assigned to an individual, because of missing or incorrect information identifying the individual or his or her military unit.

Through use of the 2000 hazard area and location data for soldiers at the company level in the Gulf region, exposure determination was provided for the 351,121 deployed Army personnel by the Office of the Special Assistant for Gulf War Illnesses. Record linkage of this chemical exposure data with the file of respondents to Phase I of the VA NHS yielded a total of 5,555 Army Gulf War veterans, who were classified into one of three categories of exposure to chemical agents, mainly sarin or cyclosarin, as follows: exposed Army Gulf War veterans, $n = 1,898$; unexposed Army Gulf War veterans, $n = 3,336$; missing exposure Army Gulf War veterans, $n = 321$.

Health Outcomes

Health perception data, before notification, were derived for all 5,555 Army Gulf War veterans who responded during Phase I of the VA NHS. The outcomes of interest are the self-assessments that were reported on the postal questionnaire developed for the VA NHS. The self-administered questionnaire was used to obtain information on the presence of various medical conditions and symptoms, measures of functional impairment, limitation of activity, and health care utilization.

A self-report symptom inventory composed of 48 items that were representative of the symptom configuration commonly

TABLE I

PREVALENCE OF SELECTED SEVERE SYMPTOMS DURING THE PAST 12 MONTHS ACCORDING TO EXPOSURE STATUS FOR 5,555 ARMY
GULF WAR VETERANS

	Prevalence (%)		
Symptoms Grouped by Organ System	Exposed (n = 1,898)	Unexposed (n = 3,336)	Adjusted Risk Ratio (95% CI)[a]
General			
Headaches	22.8	21.6	1.03 (0.93–1.15)
Runny nose	22.2	20.7	1.05 (0.94–1.17)
General muscle aches/cramps	12.2	13.7	0.88 (0.76–1.02)
Excessive fatigue	18.4	17.6	1.03 (0.91–1.16)
Fatigue >24 hours after exertion	10.1	10.6	0.94 (0.79–1.11)
Sleep difficulty	17.3	17.7	0.98 (0.87–1.11)
Sleepiness during daytime	11.1	11.5	0.96 (0.82–1.13)
Awaken tired or worn out	16.1	18.0	0.90 (0.79–1.02)
Fever or chills	4.3	4.1	1.05 (0.80–1.37)
Sweating not attributable to exercise	7.1	6.0	1.19 (0.96–1.48)
Skin, hair, and nails			
Skin rash	14.5	14.8	0.98 (0.85–1.12)
Hair loss	6.3	5.9	1.06 (0.85–1.32)
Ears			
Hearing loss	8.8	8.6	1.04 (0.87–1.25)
Mouth and throat			
Mouth, teeth, or gum problems	13.8	13.1	1.05 (0.91–1.21)
Sore throat or hoarse voice	10.9	9.8	1.08 (0.92–1.28)
Trouble swallowing	4.2	4.1	1.01 (0.77–1.33)
Respiratory			
Wheezing	6.7	8.2	0.81 (0.66–1.00)
Coughing	8.9	8.9	1.00 (0.83–1.20)
Breathing or shortness of breath	9.9	10.1	0.97 (0.82–1.15)
Cardiac			
Irregular heartbeat	5.1	5.7	0.88 (0.69–1.12)
Gastrointestinal			
Nausea	5.8	5.0	1.14 (0.90–1.44)
Vomiting	3.4	2.7	1.28 (0.93–1.75)
Stomach or abdominal pain	11.7	10.8	1.06 (0.90–1.24)
Reflux, heartburn, or indigestion	13.6	14.5	0.94 (0.82–1.08)
Diarrhea	11.8	11.3	1.07 (0.91–1.25)
Constipation	3.6	4.0	0.87 (0.65–1.16)
Genitourinary/reproductive			
Frequent/painful urination	4.2	4.4	0.91 (0.70–1.19)
Painful sexual intercourse	2.7	2.2	1.16 (0.81–1.65)
Impotence or other sexual problems	3.9	4.7	0.85 (0.65–1.12)
Musculoskeletal			
Back pain/spasms	20.2	20.9	0.97 (0.87–1.08)
Joint aches or pain	20.4	22.0	0.93 (0.83–1.04)
Swelling in any joints	6.8	8.6	0.79 (0.65–0.97)
Hematological			
Bruise or bleed easily	3.1	3.0	1.00 (0.73–1.37)
Sensory/neurological			
Loss of balance/dizziness	5.9	5.8	1.00 (0.80–1.26)
Blurred vision	4.2	4.6	0.90 (0.69–1.18)
Speech difficulty	1.7	2.1	0.77 (0.51–1.16)
Sudden loss of strength	6.6	5.9	1.12 (0.90–1.39)
Concentration/memory problems	13.8	12.8	1.06 (0.92–1.23)
Numbness in hands/feet	11.6	12.1	0.95 (0.82–1.11)
Tremor/shaking	3.5	3.9	0.89 (0.67–1.20)
Psychiatric			
Anxious, irritable, or upset	19.1	19.1	0.99 (0.88–1.11)
Been depressed or blue	16.1	15.0	1.06 (0.93–1.21)
Immunological			
Sensitive to chemicals	7.1	7.3	0.94 (0.77–1.15)
Lymphatic			
Swollen glands	5.0	5.5	0.89 (0.70–1.14)
Other (symptom meets the criteria for more than one category)			
Tightness in chest	6.2	7.1	0.87 (0.70–1.08)
Swelling of feet/ankles	4.5	5.2	0.84 (0.65–1.08)
Wound slow to heal	3.5	3.3	1.03 (0.77–1.40)

[a] Adjusted risk ratios (and 95% confidence intervals [CIs]) from Cochran-Mantel-Haenszel analysis, with adjustment for age, gender, race, rank, marital status, and unit component.

observed among outpatients was used to assess the prevalence of somatic and psychological symptoms. Complete lists of symptoms (Table I), grouped according to organ system, and conditions (Table II) are presented.

Questionnaire items were used to evaluate limitation of activity, prevalence of chronic conditions, self-assessed health status, and use of medical services, including physician contacts related to illness (excluding routine visits for vaccinations and physical examinations) and hospitalizations overnight. The PTSD Checklist, which was part of the survey instrument, contained 17 questions concerning PTSD symptoms experienced in the past 1 month.[17] A cutoff score of ≥50 points was used to classify veterans as having PTSD.[18] Participants were classified regarding the presence of chronic fatigue syndrome (CFS). The case definition that had been coordinated by the Centers for Disease Control and Prevention in 1994[19] was modified in terms of the time period for duration of symptoms that was available on the NHS survey instrument. This modification was described and evaluated elsewhere and is termed CFS-like illness.[20] Questions on smoking history and alcohol use were included, as well as weight change in the past 6 months. All of these outcomes were fully described elsewhere for the entire cohort of 11,441 Gulf War respondents and 9,476 non-Gulf War respondents.[2]

Demographic Characteristics and Military Variables

Basic demographic data and military variables (date of birth, gender, marital status, race, branch, rank, military occupational specialty code, and unit component) were derived from Defense Manpower Data Center (DMDC) and VA records. Date of birth, gender, and marital status were also investigated with the survey instrument. Gender, a binary variable, was coded as male vs. female. Age at the time of the Gulf War (1991) was recoded from the DMDC database as a binary variable, i.e., <30 years vs. ≥30 years. Race/ethnicity was coded into three strata, i.e., (1) Caucasian, (2) African American, or (3) Hispanic, American Indian, Alaskan Native, Asian, Pacific Islander, any other, or missing. Marital status at the time of the Gulf War, from the DMDC file, was converted to a binary variable, i.e., single vs. ever married. Rank at the time of the Gulf War was coded as a binary variable, i.e., enlisted vs. officer or warrant officer. Unit component was coded into three strata, i.e., Army active, Army National Guard, or Army Reserve.

Statistical Methods

Analyses measured the association between presumed exposure to chemical agents and the various health outcomes described in the survey instrument. We used contingency table

TABLE II

PREVALENCE OF SELECTED SELF-REPORTED MEDICAL CONDITIONS DURING THE PAST 12 MONTHS ACCORDING TO EXPOSURE STATUS FOR 5,555 ARMY GULF WAR VETERANS

Conditions	Prevalence (%)		Adjusted Risk Ratio (95% CI)[a]
	Exposed (n = 1,898)	Unexposed (n = 3,336)	
Arthritis	29.4	29.0	1.02 (0.93–1.11)
Lumbago	19.9	20.1	0.98 (0.88–1.10)
Diseases of muscles or tendons	10.3	10.4	0.98 (0.83–1.15)
Skin cancer	3.3	2.6	1.30 (0.94–1.79)
Other cancer	1.0	1.4	0.67 (0.40–1.12)
Eczema or psoriasis	10.5	9.5	1.11 (0.93–1.31)
Other dermatitis	35.6	34.2	1.03 (0.95–1.11)
Diseases of the hair or scalp, hair loss	22.6	21.5	1.05 (0.94–1.16)
Cirrhosis of liver	0.7	0.4	2.07 (0.97–4.42)
Hepatitis	1.7	1.3	1.32 (0.84–2.06)
Other liver disease	2.0	1.7	1.11 (0.74–1.67)
Gastritis	32.7	31.3	1.04 (0.96–1.13)
Enteritis	9.8	8.0	1.19 (1.00–1.43)
Colitis	8.6	6.0	1.39 (1.14–1.70)
Frequent diarrhea	29.6	28.9	1.03 (0.95–1.13)
Diabetes mellitus	1.3	1.4	0.92 (0.57–1.48)
Other endocrine disorder	2.6	2.6	0.92 (0.65–1.30)
Repeated seizures	3.1	3.5	0.89 (0.66–1.22)
Recurrent headaches	44.5	43.8	1.01 (0.95–1.08)
Migraines	20.0	21.3	0.93 (0.83–1.04)
Neuralgia or neuritis	6.8	6.4	1.05 (0.85–1.30)
Any disease of genital organs	6.3	6.6	0.94 (0.76–1.17)
Heart disease	1.8	1.8	0.98 (0.64–1.48)
Hypertension	15.1	14.8	1.03 (0.90–1.18)
Stroke	0.5	0.6	0.89 (0.42–1.88)
Tachycardia	11.9	12.7	0.92 (0.79–1.07)
Sinusitis	48.8	47.8	1.01 (0.96–1.07)
Bronchitis	15.1	14.5	1.02 (0.89–1.16)
Asthma	6.6	5.8	1.10 (0.88–1.37)
Other lung condition	6.8	7.3	0.96 (0.78–1.18)
Bladder infection	7.1	6.8	0.98 (0.80–1.20)

[a] Adjusted risk ratios (and 95% confidence intervals [CIs]) from Cochran-Mantel-Haenszel analysis, with adjustment for age, gender, race, rank, marital status, and unit component.

<div align="center">TABLE III</div>

PERCENTAGE DISTRIBUTION OF SELECTED DEMOGRAPHIC/MILITARY SERVICE CHARACTERISTICS AMONG 5,555 ARMY GULF WAR VETERANS ACCORDING TO POSSIBLE EXPOSURE TO CHEMICAL AGENTS

Characteristics	Exposed[a] (n = 1,898)		Unexposed (n = 3,336)		Missing Exposure (n = 321)	
	No.	%	No.	%	No.	%
Gender						
Male	1,425	75.1	2,631	78.9	252	78.5
Female	473	24.9	705	21.1	69	21.5
Age (years) (mean in 1991)	31.0		30.9		29.8	
Interquartile range (years)	24–37		24–37		24–34	
Race						
Caucasian	1,363	71.8	2,405	72.1	237	73.8
African American	375	19.8	716	21.5	64	19.9
Hispanic	96	5.1	137	4.1	10	3.1
Other[b]	61	3.2	72	2.2	9	2.8
Missing	3	0.2	6	0.2	1	0.3
Marital status						
Married	1,006	53.0	1,760	52.8	155	48.3
Single	774	40.8	1,380	41.4	148	46.1
Other	118	6.2	196	5.9	18	5.6
Rank						
Enlisted	1,623	85.5	2,926	87.7	276	86.0
Officer	241	12.7	351	10.5	44	13.7
Warrant	34	1.8	59	1.8	1	0.3
Unit component						
Active	491	25.9	954	28.6	81	25.2
National Guard	742	39.1	1,328	39.8	32	10.0
Reserve	665	35.0	1,054	31.6	208	64.8

[a] Total (n = 5,555) is composed of possibly exposed (n = 1,898) plus unexposed (presumed not in hazard area) (n = 3,336) plus missing exposure status (n = 321). Possibly exposed is based on the DoD revised 2000 hazard area.

[b] Race "other" includes American Indian, Alaskan Native, Asian, Pacific Islander, and any other.

analysis to examine differences with respect to demographic and military factors between exposed and unexposed Army Gulf War veterans. Unadjusted risk ratios (relative risk) were calculated directly from the raw table entries. Adjusted risk ratios included adjustments for age in 1991 (<30 years vs. ≥30 years), gender, race/ethnicity (Caucasian, African American, or all other, including Hispanic), marital status (single vs. all other), rank (enlisted vs. officer or warrant officer), and Army active duty vs. Army Reserve or National Guard service. These adjustment factors were chosen based on their potential association with health outcomes. We adjusted for these factors using a propensity score,[21] which, divided into quintiles, was used to stratify the Cochran-Mantel-Haenszel analyses. Statistical significance was ascertained by examining the coverage of 95% confidence intervals, and no adjustments were made for multiple comparisons. Computations were carried out with standard software.[22]

Imputation

To avoid losing observations because of missing demographic and military data in the DMDC data file, we extracted the corresponding items from the NHS Phase I postal questionnaire, when possible. For the few cases of missing values for the race variable for which this approach did not work (n = 10), we created a category of "missing" for the crude rates but pooled the 10 missing observations with the "other" race stratum for the calculation of adjusted risk ratios. No imputation was performed for item nonresponses regarding outcome variables.

Sensitivity Analyses

Because 5.7% of the Army Gulf War veterans had missing exposure data, a sensitivity analysis was conducted for the main outcomes, to assess the potential effect of these missing data. First, subjects in the unknown exposure group were added to the exposed group and compared with unexposed subjects. Second, subjects in the missing exposure group were added to the unexposed group and compared with exposed subjects.

Institutional Review Board Approval

This project was submitted for institutional review board review, and approval was obtained from both the Department of Veterans Affairs and the National Academy of Sciences.

Results

Characteristics of Exposed and Unexposed Army Gulf War Veterans

The demographic and military characteristics of the 5,555 Army Gulf War veterans are presented in Table III, categorized by the three levels of exposure to chemical agents. The exposed group had a greater proportion of female veterans than did the unexposed group (24.9% vs. 21.1%; p < 0.01) and differed by race, having fewer African American veterans (19.8% vs. 21.5%) and a greater proportion of "other" races (Hispanic, American Indian/Alaskan, or Asian/Pacific Islander) (8.3% vs. 6.3%) than the unexposed group (p = 0.013). Regarding unit component,

there was a greater proportion of reservists in the exposed group than in the unexposed group (35.0% vs. 31.6%; p = 0.02). There were no significant differences between the exposed and unexposed groups for the variables age, marital status, and rank.

Functional Impairment, Limitation of Work, and Medical Care Utilization Attributable to Illness

Approximately the same percentages of exposed Army Gulf War veterans and unexposed Army Gulf War veterans reported staying home all or part of a day because they did not feel well or as a result of illness or injury within the 2 weeks before the survey response (31.0% vs. 31.9%) (Table IV). The percentage distribution of number of days at home during the past 2 weeks is shown for both groups; there was no difference between these two distributions (p = 0.15). Similarly, 20.9% of exposed Gulf War veterans and 22.0% of unexposed Gulf War veterans reported that they were limited in employment or in the kind of work they could do around the house because of an impairment or health problem (p = 0.36). Less than 2% of the respondents did not answer either of these two questions. There was no difference between the exposed and unexposed groups in the number of clinic or doctor visits made during the past 12 months because of illness (p = 0.62). Approximately 6% of each group did not answer this question. Among the exposed veterans, 8.9% reported having been hospitalized overnight or longer for illness during the past 12 months, whereas the corresponding percentage among

unexposed veterans was 9.2%. The percentage distributions of those hospitalized were not different between the two groups (p = 0.88). Item nonresponse rates for this question were 3.4% for the two groups.

Sensitivity Analyses

In Table V, we assumed that all Army Gulf War veterans with missing exposure data were actually exposed. We consequently found no statistically significant differences for functional impairment (bed days), limitation of employment, number of clinic or doctor visits, or number of hospitalizations. Conversely, when we assumed that the veterans with missing exposure data were actually unexposed (Table VI), we reached the same conclusion. Because these results are the same as those in Table IV, we excluded subjects with missing exposure data from the remainder of the analyses in Tables I, II, VII, VIII, and IX.

Perception of General Health

There was no difference in perception of general health status between exposed and unexposed veterans (p = 0.72; Table VII). The item nonresponse rate for this question was 14% for each group, which is higher than rates for other items in the survey because the physical placement of this item on the survey form meant that it was inadvertently skipped by participants.

TABLE IV

PERCENTAGE DISTRIBUTION OF FUNCTIONAL IMPAIRMENT, LIMITATION OF EMPLOYMENT, AND MEDICAL CARE UTILIZATION ATTRIBUTABLE TO ILLNESS AMONG 5,555 ARMY GULF WAR VETERANS ACCORDING TO EXPOSURE STATUS

Conditions	Exposed (n = 1,898)		Unexposed (n = 3,336)		Missing Exposure (n = 321)		p^a
	No.	%	No.	%	No.	%	
Functional impairment							
Bed days							
0	1,291	69.0	2,235	68.1	207	64.9	
1–2	352	18.8	602	18.4	71	22.3	
3–4	125	6.7	277	8.4	25	7.8	
≥5	102	5.5	167	5.1	16	5.0	
Not answered[b]	28		55		2		0.15
Limitation of employment							
No	1,479	79.1	2,568	78.0	258	81.1	
Yes	391	20.9	724	22.0	60	18.9	
Not answered[b]	28		44		3		0.36
Clinic visit during past 12 months							
None	760	42.9	1,398	44.3	133	44.3	
1–3	563	31.8	974	30.9	88	29.3	
4–6	238	13.4	437	13.8	38	12.7	
≥7	211	11.9	347	11.0	41	13.7	
Not answered[b]	126		180		21		0.62
Hospitalization during past 12 months							
None	1,669	91.1	2,926	90.8	286	93.2	
1	123	6.7	213	6.6	15	4.9	
2	28	1.5	59	1.8	5	1.6	
≥3	13	0.7	24	0.7	1	0.3	
Not answered[b]	65		114		14		0.88

[a] p, significance probability by χ^2 test of independence between exposure categories (known exposed vs. known unexposed) and health condition indicator.

[b] "Not answered" category is presented for interest but is not included in the denominator in calculation of percentages.

TABLE V

SENSITIVITY ANALYSIS WITH 321 VETERANS WITH MISSING EXPOSURE STATUS INCLUDED IN THE CATEGORY OF EXPOSED: PERCENTAGE
DISTRIBUTION OF FUNCTIONAL IMPAIRMENT, LIMITATION OF EMPLOYMENT, AND MEDICAL CARE UTILIZATION ATTRIBUTABLE TO ILLNESS

Conditions	Exposed + Missing Exposure ($n = 1,898 + 321$)		Unexposed ($n = 3,336$)		p^a
	No.	%	No.	%	
Functional impairment					
Bed days					
0	1,498	68.4	2,235	68.1	
1–2	423	19.3	602	18.4	
3–4	150	6.9	277	8.4	
≥5	118	5.4	167	5.1	0.16
Not answered[b]	30		55		
Limitation of employment					
No	1,737	79.4	2,568	78.0	
Yes	451	20.6	724	22.0	0.22
Not answered[b]	31		44		
Clinic visit during past 12 months					
None	893	43.1	1,398	44.3	
1–3	651	31.4	974	30.9	
4–6	276	13.3	437	13.8	
≥7	252	12.2	347	11.0	0.52
Not answered[b]	147		180		
Hospitalization during past 12 months					
None	1,955	91.4	2,926	90.8	
1	138	6.4	213	6.6	
2	33	1.5	59	1.8	
≥3	14	0.7	24	0.7	
Not answered[b]	79		114		0.83

[a] p, significance probability by χ^2 test of independence between exposure category and health condition indicator.

[b] "Not answered" category is presented for interest but is not included in the denominator in calculation of percentages.

Prevalence of Severe Symptoms

On the survey instrument, the veteran was given the guideline for reporting a symptom experienced during the past year as "severe" if its presence was "sufficient to seek medical advice, take prescription drugs, lose work, or limit routine activities." The prevalences of severe symptoms for exposed and unexposed veterans are presented in Table I for 47 symptoms (one symptom pertained only to male veterans and was excluded). The adjusted risk ratios showed two statistically significant associations between exposure and self-reported severe symptoms, i.e., the rates of wheezing and of swelling in any joints were lower in the exposed group. Because one would expect 1 of 20 statistical tests performed at the $p = 0.05$ level to be statistically significant by chance, the finding of two significant risk ratios in 47 tests could well be attributable to chance alone.

Prevalence of Mild or Severe Symptoms

On the survey instrument, the veteran was given the guideline for reporting a symptom experienced during the past year as "mild" if its presence caused the veteran to be "just aware but not slowed down by symptoms, or sufficient to take nonprescription drugs to relieve the symptoms (aspirin, Tums, etc.)." The prevalence of either mild or severe symptom was computed for each of the 47 symptoms, and results were compared for exposed and unexposed veterans. The adjusted risk ratios were not materially different from those for severe symptoms.

Prevalence of Chronic Medical Conditions

The prevalences of 31 medical conditions during the past 12 months are shown in Table II for exposed and unexposed veterans. Of the 31 medical conditions in Table II, all except two showed the same rates in the exposed and unexposed groups; enteritis and colitis had significantly higher rates in the exposed group. Again, because one would expect 1 of 20 statistical tests performed at the $p = 0.05$ level to be statistically significant by chance, the finding of two significant risk ratios in 31 tests could well be attributable to chance alone.

In Table VIII, the prevalences of two symptom-based medical conditions, PTSD and CFS-like illness, are tabulated. There was no significant difference in the prevalence of either medical condition according to exposure status.

Alternative Measures of Exposure

Next, we examined the relationship between number of days of possible exposure to chemical agents from March 10 to 13, 1991, coded as 0, 1, or ≥2 days, and general health status, number of clinic or doctor visits, number of hospitalizations, PTSD, and CFS-like illness (Table IX). The χ^2 tests showed no relationships between the number of days exposed (coded as 0, 1, or ≥2) and any of the health status indices ($p > 0.50$). Finally, using an alternative definition of exposure based on the 50-km proximity, i.e., within the 50-km radius from Khamisiyah from March 10 to 13, 1991, we assessed the frequency distributions of the same health indices (Table X). The χ^2 tests showed no

TABLE VI

SENSITIVITY ANALYSIS WITH 321 VETERANS WITH MISSING EXPOSURE STATUS INCLUDED IN THE CATEGORY OF UNEXPOSED: PERCENTAGE DISTRIBUTION OF FUNCTIONAL IMPAIRMENT, LIMITATION OF EMPLOYMENT, AND MEDICAL CARE UTILIZATION ATTRIBUTABLE TO ILLNESS

Conditions	Exposed (n = 1,898)		Unexposed + Missing Exposure (n = 3,336 + 321)		p^a
	No.	%	No.	%	
Functional impairment					
Bed days					
0	1,291	69.0	2,442	67.8	
1–2	352	18.8	673	18.7	
3–4	125	6.7	302	8.4	
≥5	102	5.5	183	5.1	0.16
Not answered[b]	28		57		
Limitation of employment					
No	1,479	79.1	2,826	78.3	
Yes	391	20.9	784	21.7	0.49
Not answered[b]	28		47		
Clinic visit during past 12 months					
None	760	42.9	1,531	44.3	
1–3	563	31.8	1,062	30.7	
4–6	238	13.4	475	13.7	
≥7	211	11.9	388	11.2	0.68
Not answered[b]	126		201		
Hospitalization during past 12 months					
None	1,669	91.1	3,712	91.0	
1	123	6.7	228	6.5	
2	28	1.5	64	1.8	
≥3	13	0.7	25	0.7	
Not answered[b]	65		128		0.88

[a] p, significance probability by χ^2 test of independence between exposure category and health condition indicator.

[b] "Not answered" category is presented for interest but is not included in the denominator in calculation of percentages.

TABLE VII

PERCENTAGE DISTRIBUTION OF PERCEPTION OF GENERAL HEALTH AS REPORTED BY VETERANS ACCORDING TO EXPOSURE TO NERVE AGENTS SARIN OR CYCLOSARIN

General Health	Exposed (n = 1,898)		Unexposed (n = 3,336)	
	No.	%	No.	%
Excellent	180	11.0	292	10.2
Very good	380	23.2	671	23.5
Good	582	35.6	1009	35.3
Fair	419	25.6	733	25.6
Poor	74	4.5	153	5.4
Not answered[a]	263		478	

Significance probability by χ^2 test of independence between exposure and general health status, $p = 0.72$, $\chi^2_4 = 2.08$.

[a] "Not answered" category is presented for interest but is not included in the denominator in calculation of percentages. The excess item nonresponse for this question is attributable to the position of the question on the survey instrument.

association between 50-km exposure defined and any of the health status indices ($p > 0.45$).

Discussion

A population-based sample of Army Gulf War veterans who participated in the NHS and who were presumed to have been exposed to chemical agents in Khamisiyah, Iraq, did not report higher rates of days spent in bed within the past 2 weeks, health limitation, or medical care utilization, as measured by outpatient office visits or inpatient hospitalizations within the past year, than did similar unexposed veterans. Similarly, the two groups perceived their health status to be the same when asked to classify themselves into one of five categories, ranging from excellent to very good, good, fair, or poor. After adjustment for possible differences in demographic/military characteristics, the subjects in the exposed and unexposed groups reported equal prevalences for 45 of 47 severe symptoms and for 29 of 31 medical conditions. We also note that, based on what is known about health effects following exposure to anticholinesterase agents, we would have expected differences in neurological and behavioral symptoms, which we did not observe.

TABLE VIII

PERCENTAGE OF SYMPTOM-BASED MEDICAL CONDITIONS ACCORDING TO EXPOSURE STATUS

	Prevalence (%)		
Medical Condition	Exposed (n = 1,898)	Unexposed (n = 3,336)	p^a
PTSD[b]	15.5	15.6	0.88
CFS-like illness	7.0	6.4	0.48

[a] p, significance probability by χ^2 test of independence between exposure and symptom-based medical condition.

[b] PTSD, $\geq$50 points by self-report on PTSD Checklist.

The accuracy of exposure measurement is always an issue in this kind of study. The fact that there have been three official exposure models to date shows that the science and technology have been evolving. Even so, there are some who doubt the accuracy of the process.[23] We were able to ascertain that the results we obtained were robust with respect to the choice of model, by performing analyses based on the most recent data, the 2000 hazard area, as well as the earliest data, the 50-km model. We also determined that our results were not likely to have been affected by missing exposure data; including veterans with missing exposure data in either the exposed group or the unexposed group had no noticeable effect on the study's results.

Regarding endpoints, there are known limitations to self-reporting. First, there is the issue of reporting bias. We note that the rates of self-reported illness we saw in this study are higher than those in the NHS.[2] This may be attributable to the fact our study population differed in some respects from the NHS. We

TABLE IX

DOSE-RESPONSE RELATIONSHIP BETWEEN NUMBER OF DAYS OF EXPOSURE AND GENERAL HEALTH, CLINIC VISITS, HOSPITALIZATIONS, PTSD, AND CFS-LIKE ILLNESS

	Rate (%) with Days of Exposure			
Health Status[a]	0 (n = 3,336)	1 (n = 1,740)	$\geq$2 (n = 158)	p^b
General health				
Excellent	10.2	11.1	9.8	
Very good	23.5	22.7	29.4	
Good	35.3	36.0	31.5	
Fair	25.6	25.9	23.1	
Poor	5.4	4.4	6.3	0.54
Clinic visits				
None	44.3	42.4	48.6	
1–3	30.9	31.9	30.4	
4–6	13.8	13.5	12.2	
$\geq$7	11.0	12.2	8.8	0.58
Hospitalizations				
None	90.8	91.1	90.7	
1	6.6	6.8	6.0	
2	1.8	1.4	2.6	
$\geq$3	0.7	0.7	0.7	0.92
PTSD present	15.6	15.4	15.8	0.98
CFS present	6.4	7.0	6.3	0.73

[a] Missing outcomes were excluded from denominators when percentages were calculated.

[b] p, significance probability by χ^2 test of independence between number of days of exposure and health status indicator.

TABLE X

PERCENTAGE DISTRIBUTION OF GENERAL HEALTH, CLINIC VISITS, HOSPITALIZATIONS, PTSD, AND CFS-LIKE ILLNESS BY EXPOSURE STATUS ACCORDING TO THE MODEL OF 50-km RADIUS AROUND KHAMISIYAH

Health Status[a]	Exposed (n = 199)	Unexposed (n = 5,356)	p^b
General health			
Excellent	8.4	10.7	
Very good	25.3	23.5	
Good	36.1	35.1	
Fair	25.9	25.7	
Poor	4.2	5.1	0.87
Clinic visits			
None	44.9	43.8	
1–3	34.6	31.0	
4–6	11.4	13.7	
$\geq$7	9.2	11.5	0.49
Hospitalizations			
None	91.6	91.0	
1	5.8	6.6	
2	2.1	1.7	
$\geq$3	0.5	0.7	0.93
PTSD present	15.7	15.4	0.94
CFS present	8.0	6.7	0.45

See text for details on exposure.

[a] Missing outcomes were excluded from denominators when percentages were calculated.

[b] p, significance probability by χ^2 test of independence between exposure and health status indicator.

included only deployed Army Gulf War veterans, and our sample had slightly greater proportions of female veterans, non-Caucasian veterans, enlisted personnel, and National Guard or Reserve personnel. Nonetheless, the rates in our study resemble more closely those for deployed personnel than the lower rates seen for nondeployed personnel.[2] Second, there are limitations in the type of health outcomes that can be ascertained by questionnaire. We note that some of the long-term health effects seen among subjects with sarin exposure at levels high enough to cause acute cholinergic reactions[15] were manifested as abnormal test results (e.g., digital symbol test of psychomotor performance and encephalograms during sleep) of unknown clinical significance, which might not have been identified if they did not correlate strongly with specific questionnaire items. Therefore, because of the limitations imposed by self-report, the lack of differences in health between exposed and unexposed subjects should not be over-interpreted.

In summary, we conclude that self-reported health among deployed Army Gulf War veterans 5 years after potential exposure to low levels of chemical agents at Khamisiyah, Iraq, did not differ according to exposure status. These results were the same regardless of which of two exposure models were used and were not affected by missing exposure data.

Acknowledgments

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